Review

Regulation of antimicrobial prescribing practices—a strategy for controlling nosocomial antimicrobial resistance

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Approximately 10% of hospital in-patients in the UK acquire nosocomial infection, with an increasing number of these infections caused by multiresistant organisms. It is essential to halt the development and spread of antibiotic resistance among hospital pathogens.

The relationship between antibiotic use and the development of antibiotic resistance in microorganisms is a subject of ongoing controversy and research. However, there is a general acceptance that control of antibiotic prescribing within hospitals is fundamental to controlling the development of nosocomial antibiotic resistance. In order to achieve this, there is a need to design and successfully implement targeted antibiotic policies based on local patterns of resistance. Traditional educational methods used alone for executing such policies have not been shown to be effective. Computer-based technology shows great promise but will require considerable resource allocation for its installation.

Of equal importance, the Infection Control Team must be given a high profile. Robust surveillance systems to gather epidemiological data on local prescribing practices, hospital infection control policy compliance, antibiotic resistance and hospital infection rates need to be set up within individual hospitals. The appointment of an anti-infective pharmacist should be considered. Delivery of an integrated antibiotic and infection control service requires a co-ordinated, multidisciplinary team approach with clear leadership. Finally, in order for any strategy to be successful, the full support of hospital management is essential.

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The concern about the development of antimicrobial resistance among organisms associated with nosocomial infection is not new.[1–3] Antimicrobial resistance within some hospital organisms however, has reached the point where currently available antimicrobial agents are no longer effective. Clinical dilemmas include an increasing number of serious infections caused by extended-spectrum beta-lactamase-producing *Enterobacteriaceae*, methicillin-resistant *Staphylococcus aureus*, vancomycin-resistant *Enterococci* and multiresistant *Acinetobacter* spp. There is a substantial increase in morbidity and mortality associated with infections caused by these resistant organisms as well as an increase in cost of patient care (prolonged hospital stay, use of more expensive antibiotics).[4,5] With approximately 10% of in-patients in the UK acquiring nosocomial infection[6], there is now, more than ever before, an urgent need for a concerted effort to control and prevent further development and spread of antimicrobial resistance within the hospital setting.[7–9]

ANTIMICROBIAL AGENT USE AND DEVELOPMENT OF ANTIMICROBIAL RESISTANCE

There have been sufficient reports of the association of antimicrobial usage in hospitals with the emergence of antibiotic resistance to implicate it as a causal factor.[4] The observations first, that antimicrobial resistance is more prevalent in bacterial strains causing nosocomial infections, and second, that those areas in the hospital with the highest antimicrobial usage have the highest prevalence of antibiotic-resistant bacteria (i.e. intensive care and burns units) lend further support to this association. In the United States, an ongoing multi-centre surveillance study, Project ICARE (Intensive Care Antimicrobial Resistance Epidemiology) is providing valuable data that will contribute to the understanding of the complex relationship between antimicrobial use and resistance.[10] There is currently no comparable study being undertaken in the UK.

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CONTROLLING ANTIMICROBIAL USE AND DECREASED RESISTANCE

It may seem intuitive that by controlling antimicrobial prescribing, a subsequent reduction in antibiotic resistance will occur. However, this is not easy to prove. Examples from the wider community lend support. A considerable reduction in the prevalence of erythromycin-resistant *Streptococcus pyogenes* in Finland was demonstrated after a national campaign to reduce the use of macrolide antibiotics.[11] Similarly, the abolition of certain antibiotics from animal feed in Denmark has led to a decline in resistance in faecal flora from food animals.[12]

Results of studies of antimicrobial control strategies in the hospital environment are equally suggestive; antibiotic control interventions have resulted in a decrease in extended-spectrum beta-lactamase-producing *Enterobacteriaceae* in both Intensive Care Unit (ICU) and non-ICU settings.[13,14] Data are often inconclusive however, not least because they are hampered by lack of standard definitions of resistance as well as variation in susceptibility testing. Data are also often collected from outbreak situations where confounding factors, such as a step up in infection control precautions, are difficult to control for. Changes in antibiotic resistance depend also upon other factors, including the intrinsic nature of the resistance mechanism in the organism, e.g. if an additional phenotypic advantage is concomitantly conferred, antibiotic resistance may persist in the absence of selective pressure.[15,16] Acknowledgement of the complicated relationship between antimicrobial use and changes in resistance in microorganisms is important particularly when communicating with clinical colleagues with regard to the issue of antibiotic control. This is a clear area for further research.

Although there is a recognized need for better data from controlled multi-centre studies, the consensus among healthcare professionals within the field of infection is that control of antimicrobial prescribing is one of the keystones to controlling antimicrobial resistance within hospitals.[7,8] Antimicrobial prescribing should be controlled, but the questions remain as to the optimal control measures and how best to implement them.

DEFINING THE PROBLEM

In order to have any useful impact upon antimicrobial prescribing and antibiotic resistance within an individual hospital, the epidemiology of prescribing practices and local antibiotic resistance patterns need to be defined. This is essential to enable identification of potential problem areas and for audit, feedback and follow-up purposes. Serial point prevalence studies to monitor prescribing practices provide a useful starting point for the quantification of antibiotic use within the hospital setting as well as for providing a reference point by which to gauge the impact of any control intervention (Dr. B. Dean, unpublished data). Many hospitals in the UK have traditionally been very poor at collecting and collating such data into a useful format.[17] Lack of administrative and information technology (IT) support, funding and resources, as well as under-recognition of the extent of the problem of poor prescribing practices are contributing factors. Within National Health Service hospitals, there are few, if any, existing organizational frameworks for the generation and processing of these sort of epidemiological data. Public health frameworks need to be promoted and expanded within the hospital setting in the UK.

STRATEGIES FOR CONTROL

Measures for restraint or control of antibiotic prescribing have historically been resisted by many physicians and surgeons in the UK and worldwide,[4,17] not least because they may be seen as a curb on or loss of autonomy for the prescriber, who is ultimately responsible for individual patient care. There is a need to understand the many determinants that shape antibiotic prescribing in order to devise and implement effective programmes to reduce inappropriate use. In the hospital setting in particular, prescribing decisions are often made by those with least clinical experience (junior on-call). The pressures of bed and staffing shortages lead to a drive to reduce in-patient stays. There are increasing numbers of patients who, either as a result of immunosuppression or the presence of indwelling prosthetic devices, are more susceptible to infection. The low threshold for prescribing either prophylactic or empirical antibiotics increases the likelihood of inappropriate antibiotic use in this patient population in particular. These factors together with (mis-)information regarding local antimicrobial resistance patterns may all contribute to the likelihood of the prescribing of unnecessary and costly broad-spectrum antibiotics.[18,19,20]

In addition, changes to the UK medical undergraduate curriculum have served to reduce the amount of time dedicated to microbiology and infection-related topics, which, in turn, may undermine their importance for the future generation of healthcare professionals.

In the UK, the medical profession has come under close public and governmental scrutiny (media coverage, government monitoring agencies: Commission for Health Improvement; National Institute for Clinical Excellence). Thus, accountability and the need to practice evidence-based medicine further provide strong arguments for curbing inappropriate and excessive antibiotic prescribing with all its attendant risks. The need for careful management of antimicrobial use must be communicated more clearly and effectively to clinical colleagues, along with acceptable policies and ways by which to implement them.[7–9]

ANTIBIOTIC POLICIES AS THE BASIS FOR GUIDING ANTIBIOTIC USE

With around 20% of the hospital drug budget in UK hospitals being attributable to antimicrobial costs,[17] antibiotic policies and control programmes based on local antimicrobial resistance patterns are the key to effecting appropriate antibiotic use within the hospital setting.[7–9] Some restriction to the spectrum and prescription of antibiotics that are included in the hospital formulary is fundamental to the development of such policies. Specific areas that may be successfully targeted for control include surgical prophylaxis (which constitutes a large proportion of hospital antibiotic use), as well as empirical and targeted treatment of commonly encountered infections (in the form of local treatment guidelines). In order for policies to be successful, they need to be acceptable to clinical colleagues (i.e. appropriate consultation prior to inception) and easily accessible (portable/electronic formats), as well as being continuously updated (in accordance with both local resistance patterns and national guidelines) and monitored for compliance.

Good communication needs to be established between laboratory staff, infectious disease professionals and clinicians. Important relevant information (changes in local sensitivity patterns, resistance rates, rates of unit-specific hospital-acquired infection) should be readily available and may facilitate implementation of policies if disseminated within a regular feedback forum.

Other aspects of antibiotic control policies include automatic stop dates, regular review of prescriptions with tailoring of therapy based on microbiological results and clinical response, limited susceptibility reporting by the laboratory, and the control of pharmaceutical sales promotions. Clearly, it is necessary to identify a person or persons within an individual hospital, to whom the responsibility of co-ordinating any control programme falls.

Inappropriate and excessive antibiotic prescribing is still a major problem within UK hospitals.[17] This is a poor reflection of our ability to implement antibiotic policies effectively.

Table 1. Steps to control development and spread of antimicrobial resistance within hospitals

Set up **multidisciplinary hospital epidemiology team** to integrate infection and antibiotic control. Include: consultant (microbiologist/infectious diseases/hospital epidemiologist); pharmacist (infectious diseases pharmacist); infection control team; BMS; data management and IT support.
Recognize that the **support of hospital administration** and leadership is mandatory: accountability for implementation of policies.
Develop **coordinated comprehensive surveillance system** for monitoring of local epidemiology of antimicrobial resistance and hospital-acquired infection and of antibiotic prescribing.
Improve antibiotic prescribing:
(a) Set up **antibiotic steering group/antibiotic committee**: responsible for (b). Must have hospital leadership backing.
(b) Develop **antibiotic policies** based upon local surveillance data: easily accessible hospital formulary; surgical prophylaxis guidelines and local treatment guidelines for commonly encountered infections; restricted range of available antibiotics; automatic stop dates; limited susceptibility reporting; control of pharmaceutical sales promotion.
(c) Implement effective **antibiotic policies**: educational campaigns; structured educational order forms; computer-assisted decision support systems; one-on-one educational outreach; requirement for prior authorization for restricted antibiotics.
Raise profile of **Infection Control Team** and its activities.
Regularly review and update policies, measurement of outcomes.
Set up **active feedback** to hospital staff: creation of formal pathway for communication between hospital epidemiology team and ward-based clinicians.

BMS, biomedical scientist

IMPLEMENTATION OF POLICIES

Current systems for implementing antibiotic policies and thus improving precision of antibiotic prescribing include both paper-based and computer-based technology (Table 1). Passive education alone (lectures, educational events, leaflets, handouts) has not been shown to be effective in improving clinical practice either in the short or long term.[18,20,21,22] In the UK this may be partly a result of the rapid turnover of junior staff and the difficulty in maintaining a continuous educational programme.[18] When passive education is combined with interactive interventions, for example active discussions with heads of clinical programmes[22] or structured educational order forms,[23] the results are considerably better.

Several computer-assisted decision support systems have been shown to be successful in guiding and monitoring antibiotic prescribing. Success has been achieved on all fronts: acceptability to clinicians, decrease in prevalence of multi-resistant organisms within specialized units, decrease in numbers of adverse drug reactions, cost reductions; all with no documented clinical adverse outcome on in-patient care.[19,24,25] Computer-based technology shows great promise but requires considerable financial and technical input, which, within the framework of the NHS (individual trust-based computer systems, interfacing problems between laboratory and ward-based systems), is not likely to be an achievable goal in the near future.

Another system is that of individual 'academic detailing',[26] which is a one-to-one educational approach programme based on established principles of behavioural science and market research and communications theory. This has been shown to be effective in improving the accuracy and appropriateness of drug prescription as well as being cost effective.

A strategy requiring prior authorization for selected antibiotic agents is employed within many hospitals within the UK and elsewhere, and has been shown to improve antimicrobial susceptibilities when implemented rigorously.[27] Again, to be successful, this approach requires close cooperation between senior and junior clinical staff.

ROLE OF AN ANTI-INFECTIVE PHARMACIST

Currently the personnel who oversee the implementation of antibiotic policies include microbiologists and infectious diseases physicians, along with the infection control team and clinical pharmacists. The British Society for Antimicrobial Chemotherapy working party report suggests expanding the role of the clinical pharmacist in the UK still further.[17] The appointment of a specialist anti-infective pharmacist within a single London hospital resulted in considerable savings within 1 year.[7] The initial remit of the pharmacist in this particular case included education and advice regarding anti-fungal use. Thus the potential for further gain in terms of improving antibiotic use in general (as well as cost savings) is vast.

An overwhelming interest following a UK national survey has resulted in the development of a network for pharmacists with an interest in anti-infective agents.[28] This is aimed at promoting the vital role of infectious disease pharmacists, the dissemination of information regarding and optimization of antimicrobial prescribing in the UK. The anti-infective pharmacist should be seen as part of an integrated and multidisciplinary team that is responsible for facilitating good antimicrobial use within hospitals.

CONTROLLING ANTIBIOTICS: ONLY PART OF THE PICTURE

Many factors lead to the development and dissemination of antibiotic resistance within nosocomial pathogens. Rationalizing the use of antimicrobial agents is only a part of the picture and cannot be viewed in isolation[29](Table 1). In order to reduce the burden of hospital-acquired infection, caused by both sensitive and resistant organisms, the rate of transmission of these organisms must be checked. Knowledge of the epidemiology of local resistance patterns and infection rates (i.e. active and ongoing surveillance) is fundamental to gauging the effectiveness of any control programmes. To this end, hospitals must be equipped with adequate IT functions and the infrastructure for record keeping and surveillance purposes. There is also a need for uniformity of antimicrobial sensitivity testing methods and application of standardized consensus definitions of infection and resistance, which will allow comparison of data between and within hospitals on a more meaningful basis.

Stringent infection control measures must be enforced in order to reduce spread of infection within hospitals.[30] The role of the Infection Control Team (ICT) must be given the importance that it deserves. Infection control campaigns have in the past, and currently, met with resistance perhaps because they are seen as punitive and separate to, rather than as a necessary part of, clinical practice. Behavioural change is a large part of infection control practice, and is notoriously difficult to effect. There seems to be a general reluctance amongst clinical staff to take responsibility for maintaining good infection control practice. Even to try to ensure compliance with basic

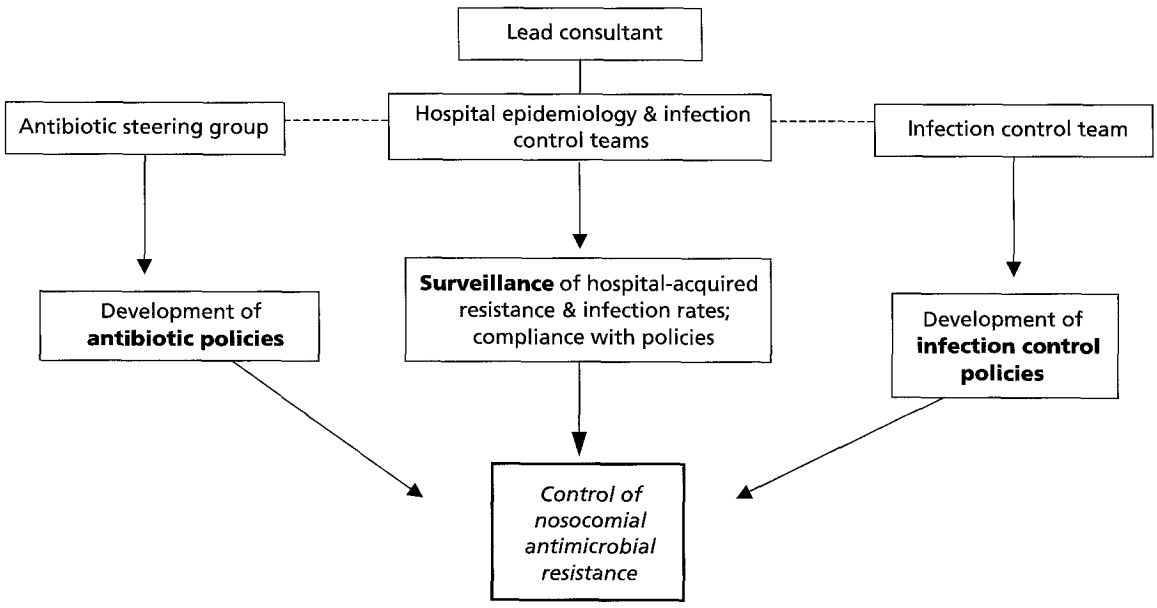

Figure 1. Coordinated multi-disciplinary approach to control of nosocomial antibiotic resistance.

hand hygiene requires a concerted effort (multidisciplinary with continuous educational campaigns), and dedication of not insignificant resources.[31]

Problems faced by ICTs are exacerbated by multiple intra-hospital patient transfers (moving an infected patient around the hospital is a sure way to disseminate nosocomial pathogens), inappropriate admissions (e.g. to cold surgical wards), staffing shortages (nursing, medical and domestic), and difficulties in ensuring or maintaining basic infection control education among locum/temporary staff. As with attempts at implementing antimicrobial control policies, ICTs are often faced with the same lack of administrative support.

The successful delivery of an integrated approach to combat nosocomial antimicrobial resistance requires coordination of the various control and surveillance systems. There needs to be a clear clinical lead—either the expansion of an existing role or the creation of a new post. Acar and Goldstein in 1998 forecast that 'a specialist in charge of bacterial resistance will be needed in hospitals to integrate ... information in order to best use antibiotics and to ensure accountability for the quality of that use'.[32] This predicted specialist role could be expanded to oversee the delivery of an integrated infection control, antimicrobial control and surveillance policy.

CONCLUSIONS

The control of antibiotic resistance within hospitals requires a coordinated multidisciplinary approach (Figure 1). Rationalization of antibiotic prescribing in the form of implementation of effective antibiotic policies is but one part of the strategy. There is a need for the development and implementation of surveillance systems for the generation and processing of relevant epidemiological data relating to antimicrobial resistance and hospital-acquired infections. There has to be in place an organizational framework for continuous monitoring of antibiotic prescribing and infection control procedure compliance and feedback. Raising the profile of infection control is a priority for all hospitals. Infection control, antibiotic control and surveillance must be integrated and co-ordinated by a team of healthcare professionals, which includes microbiologists, infectious disease physicians, the ICT, pharmacists, data management and IT resources, but with a clear line of accountability to a lead person. The appointment of an anti-infective pharmacist to the team should be given serious consideration. Finally, the successful implementation of any strategy for the control of antimicrobial resistance within the hospital setting is dependent upon the support and commitment of the hospital leadership and administration.

Success depends upon the hospital leadership—making the campaign against antimicrobial resistance a strategic priority and marshalling a multi-disciplinary prevention and control programme under the aegis of the hospital's overall efforts to improve quality.[29]

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